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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,373	12/28/2000	Peter Lind	008USPHRM300	7317
34135	7590	02/06/2003	EXAMINER	
COZEN O' CONNER, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508			LANDSMAN, ROBERT S	
ART UNIT	PAPER NUMBER	16		
DATE MAILED: 02/06/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Applicant No.	Applicant(s)
	09/750,373	LIND ET AL.
Examiner	Art Unit	
Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 26 November 2002.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-89 is/are pending in the application.
- 4a) Of the above claim(s) 34-89 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-33 is/are rejected.
- 7) Claim(s) 1-33 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
- Certified copies of the priority documents have been received.
  - Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)                    4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                    5) Notice of Informal Patent Application (PTO-152)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,8,9,11,12                    6) Other: *Sequence Comparisons A and B*.

## **DETAILED ACTION**

### ***1. Formal Matters***

- A. The Information Disclosure Statement, filed 5/3/01, has been entered into the record.
- B. The Information Disclosure Statement, filed 8/27/01, has been entered into the record.
- C. The Information Disclosure Statement, filed 1/4/02, has been entered into the record.
- D. The Information Disclosure Statement, filed 6/20/02, has been entered into the record.
- E. The Information Disclosure Statement, filed 9/13/02, has been entered into the record.
- F. Claims 1-89 were pending in this application and were subject to restriction in Paper No. 10, dated 5/30/02. In Paper No. 15, filed 11/26/02, Applicants elected Group I, claim 1-33 insofar as they read on SEQ ID NO:11 and 25. Therefore, claims 1-33 are the subject of this Office Action.

### ***2. Information Disclosure Statement***

- A. Reference AQ on the IDS filed 5/3/01, has been lined through since no date has been provided.
- B. Reference AA on the IDS filed 1/4/02, has been lined through since a PCT Search Report is not proper subject matter for an IDS.

### ***3. Title***

- A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. First, the word “novel” should be removed since all patents claim novel subject matter. Second, the title recites “receptors” whereas the claims are drawn to nucleic acid molecules encoding these receptors.

### ***4. Claim Objections***

- A. Claims 1-33 are objected to since they recite, or depend from claims that recite, non-elected SEQ ID NOs.
- B. Claims 1-33 are also objected to since they recite, or depend from claims that recite, “nGPCR-x.” It is suggested that the specific GPCR be recited in place of the term “nGPCR-x.”
- C. The syntax of claim 24 can be improved by inserting the word “said” between “wherein” and “mammalian cell.”

**5. Claim Rejections - 35 USC § 101**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 1-33 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to nucleic acids of SEQ ID NO:12 and which encode, or are homologous to, SEQ ID NO:25. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

It is clear from the instant specification that the claimed receptor is what is termed an “orphan receptor” in the art. The instant application does not disclose the biological role of the claimed protein or its significance. Applicants disclose in the specification that the claimed receptor is believed to be a G protein-coupled receptor. However, the basis that the receptor of the present invention is a 7 transmembrane, GPCR is not predictive of a use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants’ claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are “useful” to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of “useful” as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed “real-world” utility. The court held that:

“The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility,” “[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field,” and “a patent is not a hunting license,” “[i]t is not a reward for the search, but compensation for its successful conclusion.”

The specification discloses that the polynucleotides of the invention encode proteins which are believed to be GPCRs. However, no comparison to any known GPCR could be found in the specification. Furthermore, even if the specification asserted that the disclosed proteins have biological activities similar to known GPCRs, this cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases.

For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotide of SEQ ID NO:12 and the protein of SEQ ID NO:25, which are only believed to be GPCRs. Therefore, the instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the

instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

**Furthermore, since the nucleic acids of the invention are not supported by a specific and substantial asserted utility or a well established utility, the vector, host cell, polypeptide and method for producing the claimed polypeptide also lack utility.**

##### **5. Claim Rejections - 35 USC § 112, first paragraph - enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- A. Claims 1-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.
- B. Furthermore, even if the claims possessed utility under 35 USC 101, they would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for the nucleic acid of SEQ ID NO:12 and the protein of SEQ ID NO:25, does not reasonably provide enablement for proteins which are "**homologous to SEQ ID NO:25**," "**fragments thereof**," or which encode "**a portion**" of SEQ ID NO:25, or polynucleotides which encode these proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence

of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all nucleic acid molecules which encode proteins which are homologous to SEQ ID NO:25, or fragments thereof. Nucleic acid molecules which encode these proteins would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:12. Similarly, these proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:25. Similarly, regarding claim 25, since Applicants have not provided a utility of the nucleic acid molecule of SEQ ID NO:12, Applicants have not enabled nucleic acid molecules comprising 10 nucleotides.

Applicants provide no guidance or working examples of nucleic acid molecules which encode proteins homologous to SEQ ID NO:25, or of any proteins homologous to SEQ ID NO:25, or fragments thereof, nor do they provide a *function* of these nucleic acid molecules, or of the proteins which they encode. Applicants have provided no guidance as to what critical residues are required to maintain the functional characteristics of the protein of SEQ ID NO:25. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional protein which is less than 100% identical to that of SEQ ID NO:25.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all nucleic acids which encode proteins which are homologous to SEQ ID NO:25, as well as fragments and portions thereof. There is also a lack of guidance and working examples of these nucleic acid molecules and proteins as well as which residues are critical for protein function. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make functional protein other than that of SEQ ID NO:25 leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

**6. Claim Rejections - 35 USC § 112, first paragraph – lack of written description**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite proteins which are “**homologous to SEQ ID NO:25**,” “**fragments thereof**,” or which encode “**a portion**” of SEQ ID NO:25, and nucleic acid molecules which encode these protein. These are genus claims. Nucleic acid molecules which encode these proteins would have one or more nucleic acid substitutions, deletions, insertions and/or additions to the polynucleotide of SEQ ID NO:12. Similarly, these proteins would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:25. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:12 and 25 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

**7. Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in–

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

A. Claims 1-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Glucksmann et al. (US 2002/015046 A1). The claims recite an isolated nucleic acid molecule of SEQ ID NO:12, or which encodes SEQ ID NO:25, homologs or fragments thereof, as well as vectors, host cell, and methods of making protein. Glucksmann et al. teach a nucleic acid molecule which is 98.8% identical to that encoding SEQ ID NO:25 of the present invention. Therefore, Glucksmann et al. teach polynucleotide encoding a homolog, or fragment of SEQ ID NO:25 (Sequence Comparison A). Glucksmann et al. also teach vectors, host cells and methods of making protein (page 17, left column; page 39, Examples 2 and 3). The RNA fragment as well as the complement of the nucleic acid of Glucksmann et al. would be immediately envisioned by one of ordinary skill in the art. The use of compositions comprising these molecules is inherent in the methods used to produce the protein (e.g. buffer).

B. Claims 1-8 and 25-28 are rejected under 35 U.S.C. 102(e) as being anticipated by NCI/NINDS-CGAP. The claims recite an isolated nucleic acid molecule of SEQ ID NO:12, or which encodes SEQ ID NO:25, homologs or fragments thereof, or nucleic acid molecules comprising at least 10 nucleotides of SEQ ID NO:12. NCI/NINDS-CGAP teach a polynucleotide which comprises numerous regions of greater than 10 bases of overlap with that of SEQ ID NO:12 of the present invention (Sequence Comparison B). Due to identical bases in both sequences, it would be expected that the polynucleotide of NCI would encode a fragment of SEQ ID NO:25.

**8. Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

A. Claims 9-24 and 29-33 rejected under 35 U.S.C. 103(a) as being unpatentable over NCI/NINDS-CGAP in view of Sibson et al. (WO 94/01548). The claims recite an isolated nucleic acid molecule of SEQ ID NO:12, or which encodes SEQ ID NO:25, homologs or fragments thereof, as well as vectors, host cell, and methods of making protein. The teachings of NCI/NINDS-CGAP are recited in the above rejection under 35 USC 102. NCI/NINDS-CGAP do not teach vectors, compositions, host cells and a method of making the protein. However, Sibson et al. do teach expression cassettes, host cells and a method of making the protein (page 7, line 39 – page 9, line 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sibson et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide of NCI/NINDS-CGAP for the purpose of transfecting a host cell as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so (pages 8-13). One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful (Sibson et al., page 10, line 38 – page 12, line 42). The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

Art Unit: 1647

***Advisory information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.  
Patent Examiner  
Group 1600  
January 30, 2003

